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14. ABSTRACT
The overall goal of this project is to improve the management of military personnel and Veterans with localized lung cancer and comorbidities. The Specific Aims are to: 1) Enhance and validate the Lung Cancer Policy Model to simulate the management and subsequent outcomes of military personnel and Veterans with early stage lung cancer and specific comorbidities; 2) Determine the optimal management and indications for lobectomy, elective limited resection, stereotactic body radiotherapy, and other treatments for military personnel and Veterans with stage I NSCLC and chronic lung or heart disease as well as by overall burden of comorbidities; and 3) Determine the optimal indications for adjuvant chemotherapy in military personnel and Veterans with stage II and IIIA NSCLC and chronic lung, heart, or renal disease and by overall burden of comorbidities.

We have completed the majority of analyses to inform the parameter estimates for our simulation models that will ultimately provide guidance regarding optimal treatment of lung cancer patients with major comorbid illnesses. Most contributing analyses involved national VA health data; we identified a cohort of >20,000 NSCLC patients and collected data on comorbidities, cancer treatments and outcomes to generate estimates of treatment complications, overall survival and quality of life. These results are currently being incorporated into the well-validated Lung Cancer Policy Model to generate specific treatment recommendations.

15. SUBJECT TERMS
Military personnel, Veterans, lung cancer, comorbidities

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INTRODUCTION:

The overall goal of this project is to improve the management of military personnel and Veterans with localized lung cancer and comorbidities. The Specific Aims are to: 1) Enhance and validate the Lung Cancer Policy Model (LCPM) to simulate the management and subsequent outcomes of military personnel and Veterans with early stage lung cancer and specific comorbidities; 2) Determine the optimal management and indications for lobectomy, elective limited resection, stereotactic body radiotherapy (SBRT), and other treatments for military personnel and Veterans with stage I NSCLC and chronic lung or heart disease as well as by overall burden of comorbidities; and 3) Determine the optimal indications for adjuvant chemotherapy in military personnel and Veterans with stage II and IIIA NSCLC and chronic lung, heart, or renal disease and by overall burden of comorbidities.

KEYWORDS:

Military personnel, Veterans, lung cancer, comorbidities

ACCOMPLISHMENTS:

What were the major goals of the project?

Major Goals	Target Dates
Enhance and validate the LCPM to simulate the management and subsequent outcomes of military personnel and Veterans with early stage lung cancer and specific comorbidities	1-12 months
Determine the optimal management and indications for lobectomy, elective limited resection, stereotactic body radiotherapy, and other treatments for military personnel and veterans with stage I NSCLC and chronic lung or heart disease as well as by overall burden of comorbidities	13-20 months
Determine the optimal indications for adjuvant chemotherapy in military personnel and Veterans with stage II and IIIA NSCLC and chronic lung, heart, or renal disease and by overall burden of comorbidities	18-24 months

What was accomplished under these goals?

1) Major activities:
    a. Analyze the VA database to obtain data regarding cancer characteristics, comorbidities, treatment patterns, treatment-related complications, and outcomes
    b. Enhance and calibrate the LCPM

2) Specific objectives:
    a. Submit to local IRBs
    b. Link different VA registries, code data regarding relevant variables
    c. Analyze the MGH-RPDR, SEER-Medicaid, VACS, NHATS, VA-SQIP, and NHS-MDR databases to obtain data regarding comorbidities, quality of life, functional status, frailty, and surgical-related complications
    d. Request HRPO/ACURO approval
    e. Estimate the prevalence of comorbidities, estimate the prevalence of functional status impairment and frailty according to the presence or absence of comorbidities, estimate rates of surgical complications and chemotherapy and RT related toxicity in patients with specific comorbidities
    f. Incorporate comorbidities and functional status into the LCPM and develop new treatment modules for limited resection and adjuvant chemotherapy
    g. Calibration and validation of the enhanced LCPM
    h. Co-author manuscript on the development and validity of the enhanced LCPM
3) Significant results/developments:
    a. All institutional IRBs and HRPO/ACURO approvals obtained
    b. Calculated descriptive statistics (Table 1) and prevalence of comorbidities for lung cancer patients in VA and MGH patient data registries

Table 1. Characteristics of Massachusetts General Hospital Lung Cancer Cohort

Characteristic	Number	Percentage
Male	11,728	48.93
Age, years		
0-44	1015	4.2
45-54	2214	9.2
55-64	4921	20.5
65-74	7290	30.4
75+	8529	35.6
Race		
White	20588	85.9
Black	566	2.4
Other	2815	11.7
Comorbid Conditions Present	7633	31.8
Comorbidity		
Chronic obstructive pulmonary disease	4800	20.0
Myocardial infarction	259	1.1
Congestive heart failure	1315	5.5
Peripheral vascular disease	863	3.6
Cerebrovascular disease	1322	5.5
Dementia	60	0.25
Paralysis	206	0.86
Diabetes	7866	7.8
Chronic renal failure	1059	4.4
Cirrhosis	129	0.54
Moderate to severe liver disease	53	0.22
Ulcer	138	0.58
Rheumatic diseases	293	1.2
AIDS	41	0.17

c. Determined baseline quality of life estimates for Veterans with comorbidities and functional status impairment and estimated prevalence of comorbidities in relation to functional status impairment and frailty using Veterans Aging Cohort Study data (Table 2)

Table 2. Estimated quality of life for Veterans by comorbidity status and functional status

Age, years	Mean SF-6D Utility Values (SD)								
	All	COPD	COPD + FSI	CAD	CAD+FSI	CHF	CHF+FSI	CKD	CKD+FSI
<50	0.74 (0.14)	0.72 (0.13)	0.64 (0.10)	0.72 (0.13)	0.61 (0.10)	0.71 (0.13)	0.64 (0.1)	0.73 (0.11)	0.64 (0.1)
50-59	0.73 (0.14)	0.70 (0.13)	0.63 (0.10)	0.70 (0.13)	0.64 (0.11)	0.71 (0.13)	0.65 (0.11)	0.70 (0.14)	0.63 (0.11)
60-69	0.78 (0.13)	0.77 (0.13)	0.71 (0.12)	0.77 (0.12)	0.70 (0.10)	0.76 (0.12)	0.71 (0.11)	0.75 (0.12)	0.71 (0.1)

d. Identified major comorbidities and calculated the rate of lung cancer treatment complications in patients with comorbidities using national VA data (Table 3)

Table 3. 30-Day Complications for Lobectomy and Limited resection amongst Veteran Lung Cancer Patients

	Lobectomy	Limited Resection
Risk Factor	Odds Ratio (95% CI)	Odds Ratio (95% CI)
CAD 30-day mortality Bleeding MI	 1.67 (1.06, 2.64) 1.97 (1.34, 2.88)	 1.53 (1.00, 2.36)
CHF (mild) Atrial fibrillation Pneumonia	 1.8 (1.31, 2.49) 1.7 (1.01, 2.87)	
CKD (stage 4/5)* 30-day mortality MI Renal failure Respiratory failure	 2.96 (1.42, 6.15) 5.56 (1.70, 18.22) 2.37 (1.16, 4.86) 	 6.43 (1.28, 32.3)

COPD		
30-day mortality	1.26 (1.04, 1.53)	2.14 (1.16, 3.95)
Atrial fibrillation	1.09 (1.02, 1.17)	
Bleeding	1.86 (1.12, 3.09)	
CVA	1.67 (1.07, 2.61)	
MI	1.50 (1.00, 2.26)	
Pneumonia	1.41 (1.29, 1.54)	
Prolonged stay	1.38 (1.28, 1.48)	1.20 (1.00, 1.45)
Reintubation	1.51 (1.37, 1.67)	1.39 (1.10, 1.77)
Renal failure	1.44 (1.05, 1.99)	
Reoperation	1.28 (1.15, 1.42)	
Respiratory failure	1.40 (1.19, 1.64)	
Sepsis	1.41 (1.24, 1.60)	
Functional Status		
30-day mortality	1.94 (1.39, 2.70)	
MI	1.92 (1.03, 3.60)	
Pneumonia	1.30 (1.04, 1.63)	
Prolonged stay	1.29 (1.06, 1.58)	1.63 (1.16, 2.29)
Post-op infection	1.49 (1.01, 2.20)	
Reintubation	1.56 (1.26, 1.94)	
Respiratory failure	1.76 (1.30, 2.37)	
Sepsis		1.75 (1.02, 3.02)

e. Determined major factors associated with background mortality and treatment complications for Veterans with lung cancer for estimation of treatment harms and benefits
f. Submitted an abstract to American Thoracic Society
g. Continue modification of LCPM to incorporate new parameters, as established by analyses denoted in item c-e above

4) Other achievements:
    a. Nothing to report

What opportunities for training and professional development has the project provided?

Patrick Yong, a medical student who is receiving training in comparative effectiveness research with our group, participated in the interpretation of the data analysis for recent results for this project. Based on the work he wrote, an abstract was recently submitted to the American Thoracic Society meeting.

How were the results disseminated to communities of interest?

Results were submitted as an abstract to American Thoracic Society for their 2018 conference.

What do you plan to do during the next reporting period to accomplish the goals?

In the next reporting period we will use the enhanced LCPM to estimate the life expectancy and QALE of patients with stage I NSCLC for all possible permutations of treatment options, comorbid illness, age, sex, histology, and tumor size. We will simulate base case scenarios for stage I NSCLC for all possible permutations.

IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

Our SEER-Medicaid approvals are still pending, we will analyze this database to obtain data regarding comorbidities, quality of life, functional status, frailty, and surgical-related complications in year 2.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

Nothing to report.

PRODUCTS:

Publications, conference papers, and presentations

Nothing to report.

Website or other internet site

Nothing to report.

Technologies or techniques

Nothing to report.

Inventions, patent applications, and/or licences

Nothing to report.

Other products

Nothing to report.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Juan Wisnivesky	No change
Keith Sigel	No change
Kimberley Stone	Project role: Data analyst Nearest person month worked: 1.8 Contribution to project: Ms. Stone has participated in biweekly conference calls to assist in planning for what analyses will be incorporated into the LCPM as well as managing and preparing new data being collected and their analyses.
Joey Kong	No change
Andrew Eckel	No change
Renda Wiener	No change
Susan Bates	No change
Andrew Bean	No change

Has there been a change in the active other support of the PD/PI or senior/key personnel since the last reporting period?

Juan Wisnivesky	No change
Keith Sigel	No change
Joey Kong	No change
Andrew Eckel	No change
Renda Wiener	No change
Susan Bates	No change
Andrew Bean	No change

What other organizations were involved as partners?

Organization name: Massachusetts General Hospital (MGH)
Location of organization: Boston, MA

Partner's contribution to the support: Dr. Kong, our collaborator from MGH, is the primary simulation modeler in this project. He has been actively involved in review of data analysis to ensure that these results will be appropriate and accurate model parameters. He is supervising the modification of the Lung Cancer Policy Model to generate treatment recommendations for Veterans and Military Personnel with lung cancer and major comorbid illnesses.

Organization name: Bedford VA Research Corporation
Location of organization: Bedford, MA
Partner's contribution to the support: Dr. Wiener is the site PI for Bedford. She has significant expertise using national data resources and has helped oversee our use of these resources in parameter analyses. Her input has been very valuable for ensuring the integrity of our analyses. National VA oncologic data has only been available in recent years, and there is little published literature regarding the use of these data. The presence of an investigator with experience using these data has been critical for the efforts of the team.

Organization name: Bronx Veterans Medical Research Foundation
Location of organization: Bronx, NY
Partner's contribution to the support: Dr. Bates is the site PI for the Bronx VA. She coordinates, along with Dr. Sigel (who is a "without compensation" VA employee), the access to national VA lung cancer data. Dr. Bates is a clinical oncologist, and provides valuable oncologic input for the project as well. She has provided important oversight regarding the clinical importance of certain findings, as they are incorporated into our simulation modeling efforts.

SPECIAL REPORTING REQUIREMENTS

Not applicable

APPENDICES

See below

Comorbid Illnesses, Functional Status and Short-term complications in Veterans Undergoing Lung Cancer Resection

Patrick Yong, BS, Juan Wisnivesky, MD, DrPH, Chun Yin Kong, PhD, Susan Bates, MD, Kimberley Stone, MPH, Renda Weiner, MD, Keith Sigel, MD, PhD
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Background

Resection is the standard therapy for early stage lung cancer. However, lung resection is associated with major complications and a 3-4% risk of perioperative mortality. Better understanding of the factors associated with surgical complications is important for making decisions regarding optimal management of lung cancer patients. In this study, we identified lung cancer patients from a national Veterans Administration (VA) cohort undergoing lobectomy or limited resection for non-small cell lung cancer (NSCLC) to determine the impact of major comorbid illnesses and functional status impairment on major surgical complications.

Methods

We linked clinical and cancer data from the Veterans Corporate Data Warehouse to surgical outcomes from the Veterans Affairs Surgical Quality Improvement Project (VASQIP) database to identify 7,021 Veterans with NSCLC, who underwent either lobectomy or limited resection within the VA system between 2000-2016. Study outcomes included 30-day mortality and other major short-term surgical complications such as myocardial infarction (MI), renal failure, and respiratory failure. We assessed the association of major comorbidities and functional status impairment on these outcomes, fitting adjusted logistic regression models controlling for age, sex and cancer stage.

Results

Overall, 5,644 (80.4%) and 1,377 (19.6%) patients underwent lobectomy and limited resection, respectively. Atrial fibrillation (17% and 14% for lobectomy and limited resection, respectively) and prolonged length of stay (15% and 10%, respectively) were the most frequent 30-day complications. In lobectomy patients, COPD was independently associated with greater 30-day mortality, prolonged length of stay, and various cardiorespiratory and renal complications. Coronary artery disease (CAD), mild congestive heart failure (CHF), and advanced (stage 4-5) chronic kidney disease (CKD) were associated with cardiorespiratory complications. Advanced CKD was independently associated with greater 30-day mortality. Impaired functional status was associated with greater 30-day mortality, prolonged length of stay, post-operative infection, and cardiopulmonary complications. In limited resection patients, COPD and CAD were associated with greater 30-day mortality. COPD was also associated with an increased risk of reintubation and prolonged length of stay. Advanced CKD was associated with renal failure and impaired functional status was associated with prolonged length of stay and sepsis.

Conclusions

Cardiopulmonary and renal co-morbidities as well as impaired functional status were predictive of 30-day mortality and perioperative complications amongst veterans who received lobectomy or limited resection for lung cancer. These factors should be considered when making clinical decisions regarding optimal management of lung cancer patients.